REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 23-33, 45 and 46 are in the case.

I. CLAIM OBJECTION

Claim 23 is objected to because the degree symbol is incorrect. This has been rectified in the present response. Withdrawal of the claim objection is respectfully requested.

II. THE OBVIOUSNESS REJECTION

23-33, 45 and 46 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Anisson *et al*. (W09513801) (Anisson) in view of Bird *et al*. (W00202102) (Bird) and Villa *et al*. (EP 1183014) (Villa). The rejection is respectfully traversed.

The specification states (page 3):

> "Currently…the only route which can ensure that appropriate concentrations of that acid reach the interior of the colon is the rectal route which, however, since it does not enable the proximal part of the colon to be reached, limits the supply.. .with the undesirable and considerable inconvenience connected with this route".

It has now been discovered, surprisingly, according to the present invention, that the combination of a short-chain fatty acid (SCFA) or salt thereof and a complex soluble sugar and/or dietary fibre, which may be administered orally, leads to a significant synergistic effect between these components leading to beneficial effects to the patient (specification, page 4). As claimed, there is provided an oral pharmaceutical or dietary

composition comprising an active ingredient and a complex sugar and/or dietary fibre. The active ingredient consists of at least one short-chain fatty acid or salt thereof, and the complex sugar and/or dietary fibre is selected from inulin, pectin, dextrin, maltodextrin or derivatives thereof. One or more pharmacologically acceptable excipients are also present. The claimed composition comprises (a) a matrix consisting of lipophilic compounds with a melting point lower than 90°C and optionally amphiphilic compounds in which the active ingredient are at least partially incorporated, (b) an amphiphilic matrix, and (c) an outer hydrophilic matrix in which the lipophilic matrix and the amphiphilic matrix are dispersed.

Anisson discloses an **ester** of a short chain fatty acid (SCFA) (acetate, propionate, butyrate) covalently linked (via an ester bond) with a carrier, for example, a carbohydrate. As noted in the Action (page 5):

> "Anisson teaches that by ingestion of an agent comprising a SCFA… covalently linked to a carrier.., the bond between the SCFA and the carrier is an ester bond, which can be hydrolyzed by the microbial flora of the large bowel.

The Action continues (page 5):

> "Bird teaches a method for delivering short chain fatty acid…the fatty acid is covalently bonded to a carrier molecule by a bond hydrolysable by bacterial hydrolases in the bowel..."

In contrast, the presently claimed invention provides a composition comprising at least one SCFA, or a salt thereof. This is a different compound to that disclosed by Anisson and Bird. As is well known in the art, a SCFA covalently bonded to another agent, such as disclosed in Anisson and Bird, corresponds to a pro-drug which is different to the compound employed in the presently claimed compositions.

The Anisson and/or Bird compositions do not contain an active SCFA, but rather a different condensed inactive compound, i.e., a composite molecule. A pro-drug is a condensed inactive compound which may be chemically transformed into the active compound by *in-situ* lysis caused by bacterial enzymes upon arrival at the release-site.

In contrast, the presently claimed composition contains at least one SCFA or a salt thereof as **single** molecule, without any link with the complex sugar and/or dietary fibre. In the present invention, the composition is a homogeneous mixture of the complex sugar and/or dietary fibre and the SCFA or a salt thereof. There is no covalent bond-esterification or lysis mechanism between the complex sugar and/or dietary fibre and the SCFA or a salt thereof in the presently claimed invention. Clearly, therefore, neither Anisson nor Bird, taken singly or in combination, suggest the invention as claimed.

The above-noted deficiencies of Anisson and Bird are not cured by Villa. In particular, Villa contains no suggestion of SCFA, complex sugars and/or fibres. Anisson, Bird and/or Villa therefore do not give rise to a *prima facie* case of obviousness.

In addition, the dietary fibres or sugars are disclosed in the cited art as a carrier, i.e., an inactive agent only used to bring the fatty acid to the colon. This is to be contrasted with the complex sugar and/or dietary fibre of the present invention which is contained in the composition to synergize with the SCFA or salt thereof, i.e., as a further active ingredient able to produce a surprising and unexpected synergistic effect with the SCFA, or salt thereof. In this regard attention is directed to the specification (paragraphs 0012-0013) which states:

> "….it has now surprisingly been found…that the combination of butyric acid itself, or a salt thereof, with a soluble fibre such as, for example, inulin in an oral formulation leads to a very significant **synergic** effect between the two components, leading to amplification of the effects that may be produced by the administration of the individual substances." (Emphasis added)

The specification continues:

> "The combination according to the invention in fact leads to a synergy of the effects of the two substances which thus make up for the energy and protective deficit due to the lack or reduced production of endogenous butyric acid".

In order to demonstrate the synergistic effect between the two components of the composition of the invention, attention is directed to Example 4 (specification, page 10) describing a clinical study demonstrating the improved effect obtained by administering a tablet containing the combination of active ingredients according to the invention with respect to the same dosage of the active ingredients taken alone (i.e., the combination of butyric acid + inulin vs. butyric acid alone or inulin alone) in the treatment of inflammatory bowel disease (IBD). The synergism is demonstrated by Table 1 and the Results section.

In light of the absence of a *prima facie* case of obviousness over the cited art for the reasons discussed above, taken with the surprising and unexpected synergistic results obtained according to the invention, one of ordinary skill in the art, as of the filing date of the application, would not have been motivated to combine Anisson, Bird and/or Villa. Even if that combination had been attempted (this is not admitted), the presently claimed invention would not have resulted or have been rendered obvious thereby.

Withdrawal of the obviousness rejection of claims 23-33, 45 and 46 over Anisson in view of Bird and Villa is respectfully requested.

Favorable action is awaited.

Respectfully submitted,

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